IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

APPLICANT	: Jackowski et al.
INVENTION	: **Plasma Protease C1 Inhibitor Biopolymer Markers Indicative of Alzheimer's Disease**
SERIAL NUMBER	: 09/991,799
FILING DATE	: November 23, 2001
EXAMINER	: Chernyshev, Olga N.
GROUP ART UNIT	: 1649
OUR FILE NO.	: 2132.086

Mail Stop Appeal Brief-Patent
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

APPLICANTS' BRIEF IN ACCORDANCE WITH 37 C.F.R. § 41.37

Applicants submit this Appeal Brief to the Board of Patent Appeals and Interferences on appeal from the decision of Examiner Olga N. Chernyshev of Group Art Unit 1649 dated September 18, 2006, finally rejecting claim 1.

TABLE OF CONTENTS

I. REAL PARTY IN INTEREST

The real party in interest is Nanogen, Inc., the assignee of record.

II. RELATED APPEALS AND INTERFERENCES

Similar appeals have also been filed by Appellants in the following applications, all applications were filed on November 23, 2001; US Application Serial Numbers 09/991,796 (attorney docket number 2132.109), 09/993,344 (attorney docket number 2132.096) and 09/994,909 (attorney docket number 2132.090), which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

III. STATUS OF CLAIMS

Claims 1 and 39-46 are pending in the application. Claims 1-38 were originally presented. Claims 2-38 were cancelled without prejudice and new claims 39-46 were added by the amendment of August 21, 2003. Claims 39-46 were withdrawn from consideration on the merits based upon a restriction requirement. The final rejection of claim 1 under both 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph is appealed. Claim 1 is shown in the attached Claims Appendix.

IV. STATUS OF AMENDMENTS

No amendments have been filed subsequent to the Final Rejection mailed on September 18, 2006.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter relates to a biopolymer marker, identified by the evaluation of a sample containing a plurality of biopolymers, which evidences a link to a specific disease state. See, specification at page 35, lines 14-18. Specifically, the biopolymer marker consists of amino acid residues 2-18 of SEQ ID NO:1 and evidences a link to Alzheimer's disease. Id. at page 45, line 23 to page 46, line 6 and Figure 1.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Whether Claim 1 is Unpatentable under 35 U.S.C. § 101 as Having No Specific and Substantial Credible Utility

1. Whether the Examiner Made a *Prima Facie* Showing that the Invention Lacks a Specific and Substantial Utility

2. Whether the Examiner Properly Held that Applicants' Asserted Utility Lacks Credibility

B. Whether Claim 1 is Unpatentable under 35 U.S.C. § 112, First Paragraph as Being Based on a Nonenabling Disclosure

1. Whether the Examiner Properly Evaluated the Application for Enablement.

VII. ARGUMENT

A. The Examiner Erred in Rejecting Claim 1 under 35 U.S.C. § 101

1. The Examiner Has Failed to Make a Prima Facie Showing that the Invention Lacks A Specific And Substantial Utility.

Claim 1, as shown in the attached Claims Appendix, stands finally rejected under 35 U.S.C. § 101. The Examiner maintains that the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility.

Applicants respectfully traverse the rejection on the grounds that the application discloses an invention having specific, substantial, well-established and credible utility by showing an invention that is useful to the public as disclosed in its current form, rather than at some future date after further research, as a peptide marker linked to Alzheimer's disease. Furthermore, Applicants have supported this utility with data specifically directed to patients having Alzheimer's disease.

The standard for satisfying the requirements for utility under 35 U.S.C. § 101 is not particularly high. In most cases, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy 35 U.S.C. § 101. *See* In re Langer, 503 F.2d 1380, 1391, 183 USPQ 297 (CCPA 1974); MPEP § 2107.02(III)(A). In other words, the Office is correct to presume that a statement of utility made by an applicant is true.

Accordingly, the Examiner should presume that the claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1) is useful as a marker for Alzheimer's disease based upon Applicants' showing in Figure 1 that the peptide is linked to Alzheimer's disease by its

differential expression in Alzheimer's disease patients as compared to age-matched control patients. A copy of Figure 1 is attached hereto as part of the Evidence Appendix.

A "specific utility" refers to a utility that is well-defined, particular and specific to the subject matter claimed. Vague expressions such as "a compound has useful biological activity" or "biological properties" are meaningless. In re Fisher, 421 F.3d 1365, 1371, 76 USPQ2d 1225 (Fed. Cir. 2005); In re Kirk, 376 F.2d 936, 941, 153 USPQ 48 (CCPA 1967); MPEP § 2107.01. For example, a general statement indicating that a marker is useful for diagnostics, such as diagnosing a disease, would be insufficient, absent a disclosure of what disease and/or condition could be diagnosed. In contrast, a statement of diagnostic utility, such as diagnosing Alzheimer's disease, would be sufficient to identify a specific utility for the invention. Thus, Applicants' statement of utility regarding the use of the claimed peptide as a marker for Alzheimer's disease constitutes a specific utility since the claimed peptide is linked to the specific condition of Alzheimer's disease.

It is well known that pathological changes in an organism are reflected by changes observed in the serum protein pattern. For example, proteins that undergo a change in expression (from the normal) are often indicative of disease. A diagnosis may be predicted based upon the similarity of an unknown sample pattern to a known pattern of disease. Mass spectrometry is a tool used to establish serum protein patterns.

Generally proteins, as collected from a serum sample, are too large to be effectively resolved by mass spectrometry and thus, are often first subjected to separation by polyacrylamide gel electrophoresis. Upon electrophoresis, the proteins contained in the sample separate into bands in specific areas of the gel according to weight and charge.

The separated protein bands which are observed and deemed to be different between two comparable states (for example, disease state vs. normal state) are excised from the gel and subjected to further fragmentation by enzymes. The resulting peptides are then collected and purified by chromatography prior to identification by mass spectrometry. The peptides undergo step-wise degradation into sequence-defining fragments, i.e. the peptides are part of the original protein found in the serum sample. The mass spectral profiles generated are composed of parts of the original protein and can be used to identify this protein.

In order for a rejection under 35 U.S.C. § 101 to be appropriate, the Examiner must demonstrate that there is a complete absence of data supporting the statements which set forth the desired results of the claimed invention. In re Cortright, 165 F.3d 1353, 1355, 49 USPQ2d 1464 (Fed. Cir. 1999).

It is respectfully submitted that the "link to Alzheimer's disease" asserted by Applicants was elucidated under real-world conditions according to the methodology set forth in the following steps:

I. isolating peptides from body fluid samples obtained from two groups of patients; a) one group known to suffer from Alzheimer's disease; and b) a group of age-matched controls (healthy in regard to Alzheimer's disease);

II. carrying out the protocols disclosed in the specification on pages 37-47;

III. comparing the expression pattern of protein bands from the two groups of patients as evidenced in gels, such as that shown in Figure 1;

IV. subjecting the noted expression pattern to the criteria as disclosed in the specification at page 11, lines 9-20;

V. selecting and excising bands that are differentially expressed between the two groups, and, submitting the peptides present within the excised bands for further fragmentation and purification followed by sequence identification by mass spectrometry.

The Applicants, using the above-described methodology in a real-world environment, thereby elucidated and identified amino acid residues 2-18 of SEQ ID NO: 1 as a fragment of plasma protease C1 inhibitor protein found in patients having Alzheimer's disease but absent in healthy, age-matched control patients, thus establishing the instantly claimed link to Alzheimer's disease evidenced by the observed differential expression.

The characteristic mass spectral profile indicative of the claimed peptide was disclosed in the Declaration under 37 C.F.R. § 1.132 filed on August 21, 2003. Mass spectral profiles are reproducible and are typically published to provide established expression patterns for reference purposes.

Thus, any skilled artisan, in a real-world context, and without significant further research, could utilize the mass spectral profile provided as a reference for comparing with mass spectral profiles of peptides obtained from an unknown sample to test the unknown sample for a link to Alzheimer's disease through comparison of expression patterns, thereby demonstrating that the specification discloses a specific and substantial utility for the claimed peptide. This mass spectral profile is a showing of factual evidence that the claimed peptide could be used as a marker for Alzheimer's disease. Thus, data has been submitted supporting the desired results of the claimed invention; i.e. a biopolymer marker for Alzheimer's disease.

Accordingly, Applicants respectfully submit that the Examiner has failed to adhere to the precedent set in Cortright by failing to establish that there is a complete absence of data supporting the statements which sets forth the desired results of the claimed invention.

The Examiner notes that in the instant case, the specification discloses the finding of differential expression of protein 2-18 of SEQ ID NO: 1 in samples of patients with AD vs. normal patients and presents an assertion that this protein 2-18 of SEQ ID NO: 1 is useful as a marker of Alzheimer's disease. The Examiner asserts that it is obvious that a skilled practitioner would have to engage in significant further research to establish what amount of the instant claimed protein is diagnostic of Alzheimer's disease. However, with regard to providing a link to Alzheimer's disease as is instantly claimed, it is well settled that an applicant is not required to provide evidence of an asserted utility as a matter of statistical certainty. Nelson v. Bowler, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980); MPEP § 2107.02.

Thus, Applicants respectfully submit that providing an amount of the claimed marker that is diagnostic for Alzheimer's disease is not necessary to establish credibility of the asserted use for the claimed peptide as a marker for Alzheimer's disease. Accordingly, Applicants respectfully submit that the Examiner's requirement for such information is improper.

A "substantial utility" is a utility that defines a "real-world" use. MPEP § 2107.01(I). "Substantial utility" refers to a significant and presently-available benefit to the public. An application must show an invention that is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research.

"In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." Fisher, 421 F.3d at 1368, *citing* Nelson , 626 F.2d at 856.

In the context of an evaluation of substantial utility, the phrase "immediate benefit to the public" must not be interpreted to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. Brenner v. Manson, 383 U.S. 519, 534-535, 148 USPQ 689 (1966). Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial utility". MPEP § 2107.01(I).

Additionally, care must be given not to find a lack of specific and substantial utility based upon the setting in which the invention is to be used. This is particularly important in biotechnology; for example, during examination of inventions to be used in a research or a laboratory setting. As the Federal Circuit noted:

> "An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact 'useful' in a patent sense. [The PTO] must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm." Fisher, 421 F.3d at 1372, *citing* MPEP § 2107.01(I).

Many research tools such as gas chromatographs, screening assays and nucleotide sequencing techniques have a clear, specific and unquestionable utility, e.g., they are useful in analyzing compounds). MPEP § 2107.01(I).

Furthermore, it has been established that usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention

becomes useful is well before it is ready to be administered to humans. If Phase II testing was required in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. *See* In re Brana, 51 F.3d 1560, 1568, 34 USPQ2d 1436 (Fed. Cir. 1995); MPEP § 2107.01(III).

The identification of the presence of the claimed peptide in Alzheimer's disease and the absence (of the claimed peptide) in an age-matched control population puts a researcher one step closer to understanding the pathogenesis of Alzheimer's disease and thus, also one step closer to improved diagnosis and treatment of Alzheimer's disease. The claimed peptide can be used immediately to screen patient populations for links to Alzheimer's disease or it can be used in further research to improve diagnosis and treatment of Alzheimer's disease. There is no question that improved diagnosis and treatment of Alzheimer's disease provides a tangible benefit to society; especially for the elderly population susceptible to the development of Alzheimer's disease. Since the claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1) has a "real-world" use in its currently available form as a marker for Alzheimer's disease, the claimed peptide thus has a substantial utility.

Accordingly, there is a critical distinction between an invention that can be used in further experimentation and research, and an invention that requires further experimentation and research before it can be used. Applicants respectfully submit that the Examiner has erroneously found the claimed invention to be the latter rather than the former.

The Examiner cites Fisher in rejecting claim 1 and attempts to draw a parallel to the instant application by asserting that, just as in Fisher - where the Board reasoned that the use of the claimed expressed sequence tags ("ESTs") for the identification of polymorphisms is not a specific and substantial utility because "[w]ithout knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage," Fisher, 421 F.3d at 1368 - the detection of peptide 2-18 of SEQ ID NO: 1 in a sample of a patient suspected of having Alzheimer's disease provides no meaningful information as to the diagnosis determination.

Applicants respectfully submit that the facts in Fisher are inapposite to those concerning the present application. Fisher's invention related to five purified nucleic acid sequences – ESTs - obtained from the leaf tissue of maize plants. As described in Fisher, an EST is a short nucleotide sequence that represents a fragment of a cDNA clone. It is typically generated by isolating a cDNA clone and sequencing a small number of nucleotides located at one end of the two cDNA strands. When an EST is introduced into a sample containing a mixture of DNA, the EST may hybridize with a portion of the DNA. Such binding shows that the gene corresponding to the EST was being expressed at the time of mRNA extraction.

Fisher disclosed in his application that the claimed ESTs may have been used in a variety of ways, including, for example, measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression, isolating promoters and identifying the presence or absence of a polymorphism. Fisher, 421 F.3d at 1368. However, Fisher made no disclosure regarding the precise structure or function of

either the genes or the proteins encoded for by those genes to which the claimed ESTs correspond. Id.

The Examiner of the Fisher application rejected the claims for lack of utility under 35 U.S.C. § 101 and lack of enablement under 35 U.S.C. § 112, first paragraph. The Board affirmed the rejections. In upholding the rejection, the Court cited the guidelines in MPEP § 2107.01(I) that state a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. The Court noted the Applicants' admission that the underlying genes had no known functions, and that "[e]ssentially, the claimed ESTs act as no more than research intermediaries that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes". Id., at 1373. Accordingly, the Court found the ESTs to be mere "objects of use-testing", upon which scientific research could be performed with no assurance that anything useful will be discovered in the end. Id., *citing* Brenner, 383 U.S. at 535. Fisher's asserted uses represented merely hypothetical possibilities, objectives which the claimed ESTs, or any other EST for that matter, could possibly achieve, but none for which they have been used in the real world. For example, Fisher asserted that the ESTs could be used to identify polymorphisms or to isolate promoters. Nevertheless, in the face of a utility rejection, Fisher did not present any evidence showing that the ESTs had been used in either way. Id. Since nothing was known about the genes or proteins corresponding to the claimed ESTs, nothing set the claimed ESTs apart from the more than 32,000 ESTs disclosed in the application or from any EST derived from any organism. Id., at 1374. In other words, any EST could be

used to isolate any promoter. Furthermore, the use of the ESTs to actually identify the associated gene would constitute significant further experimentation, rendering the ESTs unable to be used in their current form. Ultimately, Fisher's ESTs were deemed only to be research intermediaries in the identification of underlying protein-encoding genes of unknown function. Id., at 1373.

In contrast to the invention of Fisher, the peptide of the instant invention is known to be a fragment of plasma protease C1 inhibitor protein having the amino acid sequence (i.e. structure) GVTSVSQIFHSPDLAIR. Furthermore, the claimed peptide is disclosed as a marker of a specific disease condition, Alzheimer's disease. Any skilled artisan, without significant further research, could utilize the mass spectral profile of the claimed peptide as a reference for comparison with mass spectral profiles obtained from an unknown sample to screen the sample for a link to Alzheimer's disease through comparison of expression patterns.

Thus, Applicants respectfully submit that the Examiner's attempt to draw a parallel between Fisher and the instant application fails to support her finding a lack of specific and substantial utility, as the facts in Fisher are not akin to the instant application.

It is clear, from consideration of all of the foregoing remarks, that the claimed invention has a specific and substantial utility. Thus, Applicants respectfully submit that the Examiner has failed to make a *prima facie* showing for lack of specific and substantial utility.

2. The Examiner Improperly Finds Applicants' Asserted Utility Lacking in Credibility

The Examiner does not doubt or dispute the results of differential expression of the instant claimed protein 2-18 of SEQ ID NO:1. The main point of disagreement appears to be the interpretation of these results and what constitutes a specific, substantial and credible utility. Thus, the Examiner appears to believe that the showing of differential expression of the claimed peptide in Alzheimer's disease as compared to expression in age-matched controls is not sufficient to indicate that the claimed peptide could be used as a marker for Alzheimer's disease.

Applicants note that it is improper for Office personnel to merely question operability. Factual reasons must be set forth which would lead one of skill in the art to question the objective truth of the statement of operability. MPEP § 2107.02(IV).

The Examiner provides her opinion on what one of skill in the art would know. For example, the Examiner states that one skilled in the art readily appreciates that detection of differentially expressed proteins represents only the first step in identification of molecules that have a diagnostic potential and that one skilled in the art readily appreciates that many factors have a link to or are associated with a particular pathological condition. However, the Examiner does not provide reasoning or references evidencing why one of skill in the art would "readily appreciate" these things.

Furthermore, the Examiner requires Applicant to provide complete characterization of the claimed peptide, including data indicating what amount of the claimed peptide is diagnostic of Alzheimer's disease, to establish a utility for the claimed peptide.

The instant situation is akin to that in Cortright. Cortright's invention was drawn to a method for treating baldness by applying Bag Balm (a commercially available product used to soften cow udders) to human scalp. The Examiner of the Cortright application rejected the claim drawn to this invention under 35 U.S.C. § 101 as lacking utility. According to the Examiner, Cortright's statement of utility, i.e. her claims of treating baldness, were not credible because baldness was generally accepted in the art as being incurable. The Examiner therefore required clinical evidence to establish the claimed utility, which Cortright did not supply. Cortright, 165 F.3d at 1355.

The Board reversed the rejection under 35 U.S.C. § 101 because the Examiner did not set out sufficient reasons for finding Cortright's statements of utility incredible. The Board additionally noted that there is no per se requirement for clinical evidence to establish the utility of any invention. Id.

Applicants respectfully submit that the Examiner has similarly erred by improperly questioning the operability of the invention, in that she states what one of skill in the art would believe without providing evidence to support her conclusion. Additionally, Applicants respectfully submit that the Examiner has further erred by requiring Applicants to provide "complete characterization" of the claimed peptide in order to establish utility since precedent dictates that evidence of absolute certainty is not required.

Compliance with 35 U.S.C. § 101 is a question of fact. Raytheon v. Roper, 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983), *cert. denied*, 469 US 835 (1984); MPEP § 2107.02(III)(A). Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, Office personnel must establish that it is more likely than

not that one of ordinary skill in the art would doubt (i.e. "question") the truth of the statement of utility. MPEP § 2107.02(III)(A). Alternatively, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. MPEP § 2164.07(I)(C).

Furthermore, an Examiner must present countervailing facts and reasoning sufficient to establish that a person of ordinary skill in the art would not believe the applicants' assertion of utility. Brana, 51 F.3d at 1568; MPEP § 2107.01(III).

The prior art recognizes that when a peptide is identified in a body fluid sample from an Alzheimer's patient or appears to be differentially expressed between an Alzheimer's disease patient and a "normal" patient (healthy with regard to Alzheimer's disease), it is immediately recognized as diagnostically valuable, even if the involvement of the peptide in the pathology of Alzheimer's disease is unknown. This practice has been known in the art since at least 1992. See, the abstract of Gunnersen et al. (Proceedings of the National Academy of Science USA 89(24):11949-11953 1992, copy attached hereto as part of the Evidence Appendix) in which the detection of glutamine synthetase in the cerebrospinal fluid of Alzheimer's disease patients lead to the suggestion of glutamine synthetase as a potential diagnostic marker for Alzheimer's disease. Since these practices are common, it is reasonable to believe that when one of skill in the art observes the differential expression of the claimed peptide between Alzheimer's disease patients and non-diseased age-matched control patients; one of skill in the art would, more likely than not, connect this peptide with potential diagnostics and/or therapeutics for Alzheimer's disease.

Furthermore, Applicants respectfully submit that one of ordinary skill in the art would find the suggestion of a link between the claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1), a fragment of plasma protease C1 inhibitor protein, and Alzheimer's disease to be reasonable because there is a known association between Alzheimer's disease and the complement system.

The C1 inhibitor protein is a regulatory molecule that inhibits complement C1 activity. See, definition of C1 INH, as accessed from the internet "immunoglossary" and attached hereto as part of the Evidence Appendix. Thus, the C1 inhibitor protein has control over the inflammatory complement cascade. See, Walker et al. Brain Research 675(1-2):75-82 1995, attached hereto as part of the Evidence Appendix.

The claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1), elucidated from and differentially expressed in diseased versus normal samples, is identified as a fragment of plasma protease C1 inhibitor protein at pages 45-46 of the specification as originally filed and is consistently replicated in the sample population. The gel shown in Figure 1 demonstrates that this peptide was identified in Alzheimer's patients but was absent in age-matched control patients.

Activation of the classical complement pathway and up-regulation of its protein components in Alzheimer's disease has been documented in the art. For example, See, Yasojima et al. American Journal of Pathology 154(3):927-936 1999, attached hereto as part of the Evidence Appendix. Additionally, the complement C1 inhibitor is known to be cleaved in Alzheimer's disease and has been found to be present in abnormal neuronal processes in Alzheimer's tissue. Id. Walker et al.

One of ordinary skill in the art would be aware of the involvement of the complement system in the pathology of Alzheimer's disease. Therefore, one of ordinary skill in the art would recognize the linkage between the claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1); complement C1 inhibitor protein and the activation of complement in Alzheimer's disease and thus would also find the suggestion of this peptide as a marker for Alzheimer's disease to be entirely reasonable.

One of ordinary skill in the art would conclude, based upon all of the foregoing remarks, that the asserted utility for the claimed peptide, use as a marker for Alzheimer's disease, is more likely than not true. Thus, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case for lack of credible utility.

B. The Examiner Erred in Rejecting Claim 1 under 35 U.S.C. § 112, First Paragraph.

1. The Examiner Improperly Finds the Invention Nonenabled

Claim 1, as shown in the attached Claims Appendix, stands finally rejected under 35 USC § 112, first paragraph.

It is well established that the enablement requirement of 35 U.S.C. § 112 incorporates the utility requirement of 35 U.S.C. § 101. Fisher, 421 F.3d at 1378. Where a written description fails to illuminate a credible utility, the PTO will make both a Section 112 rejection for failure to teach how to use the invention and a Section 101 rejection for lack of utility. Cortright, 165 F.3d at 1355. "If [certain] compositions are in fact useless, [a] specification cannot have taught how to use them." Id..

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. § 101. As the Court of Customs and Patent Appeals stated in In re Langer:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope. Langer, 503 F.2d at 1391 (emphasis in original).

The "Langer" test for utility has been used in evaluation of rejections under 35 U.S.C. § 112, first paragraph, where the rejection is based on a deficiency under 35 U.S.C. § 101. An examiner cannot make this type of rejection, however, unless it has reason to doubt the objective truth of the statements contained in the written description. Cortright, 165 F.3d at 1357. A reason to doubt an asserted utility may be established when the description "suggests an inherently unbelievable undertaking or involves implausible scientific principles." Brana, 51 F.3d at 1566.

In the present application, the Examiner rejects Claim 1 under 35 U.S.C. § 112, first paragraph, "since the claimed invention is not supported by either a clear asserted utility or well established utility for the reasons set forth [in the Examiner's rejection under 35 U.S.C. § 101] . . . one skilled in the art clearly would not know how to use the claimed invention." Applicants respectfully traverse the rejection as Applicants have established in the above remarks that the claimed invention has a specific and substantial credible utility.

A skilled artisan could easily follow the methodology for elucidating the presence of the claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1), as disclosed in the

patent application (and reiterated *supra*), on a non-differentiated patient population, in order to discern members of the population who manifest Alzheimer's disease.

Thus, one of skill in the art clearly would know how to use the claimed peptide (amino acid residues 2-18 of SEQ ID NO: 1) as a marker for Alzheimer's disease. Therefore, Applicants respectfully submit that the Examiner has failed to properly establish lack of enablement.

VIII. CONCLUSION

In conclusion, in light of the foregoing, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case for lack of utility and lack of enablement in the present application. Favorable reconsideration of this application and withdrawal of the rejections of claim 1 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph is courteously requested.

Respectfully submitted,

McHALE & SLAVIN, P.A.
2855 PGA Boulevard
Palm Beach Gardens, FL 33410
Tel.: (561) 625-6575
Fax: (561) 625-6572

By: Ferris H. Lander
Ferris H. Lander
Registration # 43,377

IX. CLAIMS APPENDIX

Claim 1. An isolated biopolymer marker consisting of amino acid residues 2-18 of SEQ ID NO:1 which evidences a link to Alzheimer's disease.

X. EVIDENCE APPENDIX

A. Figures

1. Figure 1 of the specification

B. Appellants rely on a declaration under 37 C.F.R. § 1.132.

1. The Declaration under 37 C.F.R. §1.132, filed on August 21, 2003, was entered into the prosecution record by the Examiner at page 5 of the Office Action mailed on November 25, 2003

C. Appellants rely on four references, all previously presented to the Examiner in the Response filed on June 27, 2005.

1. Gunnersen et al. Proceedings of the National Academy of Science USA 89(24):11949-11953 1992

2. Definition of "C1 INH" as accessed from the internet at the site "Immunoglossary"

3. Walker et al. Brain Research 675(1-2):75-82 1995

4. Yasojima et al. American Journal of Pathology 154(3):927-936 1999

Copies of the above-referenced figure, declaration and references are attached hereto as forms the Evidence Appendix.

XI. RELATED PROCEEDINGS APPENDIX

NONE.

There have been no decisions rendered by a court or the Board in the related proceedings identified at Section II, page 5 of this paper.